

Supplementary

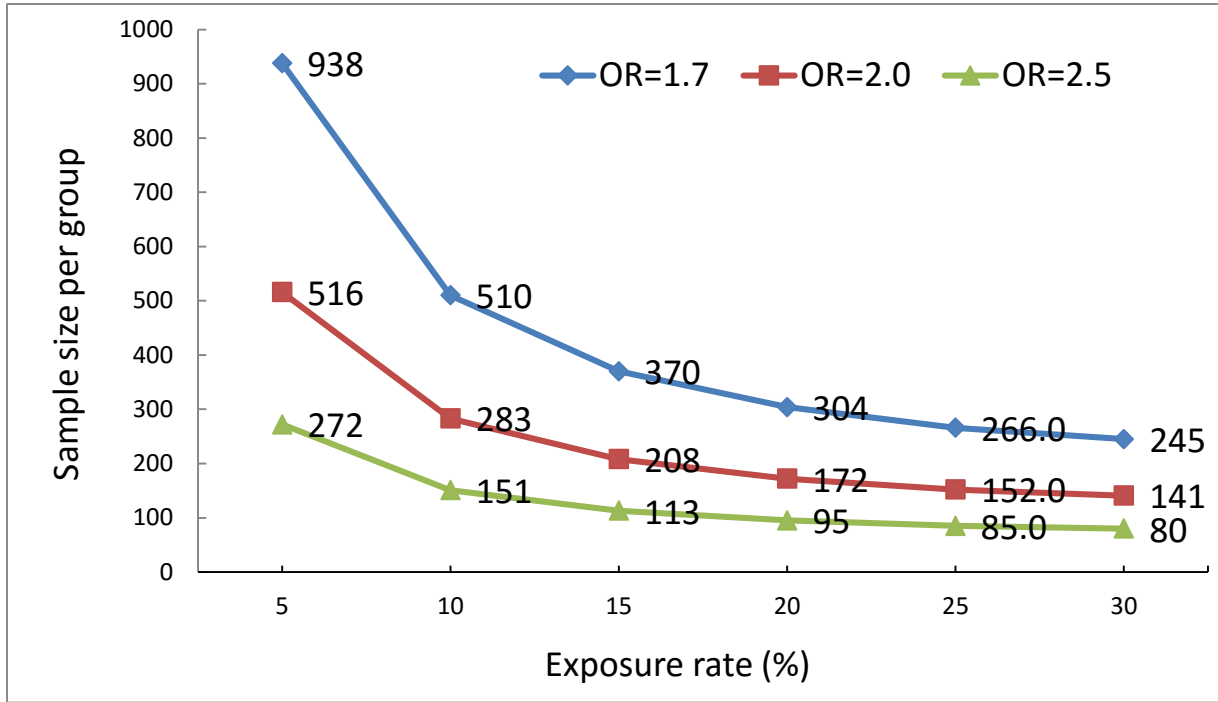


Figure S1. Sample size estimation for a case-control design under variable effect size and rate of exposure at significance level of 0.05

Table S1. Descriptive statistics of age for children and parents

		Discovery (South)						Replication (North)					
		N	Mean	Med	SD	Min	Max	N	Mean	Med	SD	Min	Max
Overall													
TD	Children's age	414	4.14	4	1.01	3	6	489	4.63	4	1.35	3	7
	Paternal age	377	35.09	35	4.52	22	59	477	34.37	34	5.12	23	59
	Maternal age	380	32.42	32	3.78	22	48	475	33.06	33	4.56	23	50
ASD	Children's age	582	4.32	4	1.13	3	7	821	4.42	4	1.10	3	7
	Paternal age	571	35.18	35	4.38	25	56	818	34.79	34	3.99	24	52
	Maternal age	578	32.49	32	3.60	21	46	819	33.09	33	3.43	25	48
Further matched by province*													
TD	Children's age	414	4.14	4	1.01	3	6	485	4.64	4	1.35	3	7
	Paternal age	377	35.09	35	4.52	22	59	473	34.39	34	5.13	23	59
	Maternal age	380	32.42	32	3.78	22	48	471	33.07	33	4.58	23	50
ASD	Children's age	152	4.30	4	1.20	3	7	550	4.29	4	1.08	3	7
	Paternal age	146	34.90	34	4.95	25	56	547	34.48	34	3.91	24	51
	Maternal age	151	31.62	32	3.66	25	43	548	32.80	33	3.37	25	45

* Statistics for samples in which both ASD and TD were recruited from the same province.

Table S2. Frequency of the overall and boys-only of the combined sample of discovery and replication (a, Fisher exact test)

Variable	Code	Category	Overall		P	Boys-only		P
			TD, n (%)	ASD, n (%)		TD, n (%)	ASD, n (%)	
Demographics								
Residence	1	City	770 (85.27)	1182 (84.25)	0.506	423 (86.68)	1011 (83.83)	0.141
	2	County	133 (14.73)	221 (15.75)		65 (13.32)	195 (16.17)	
Gender	1	Boy	488 (54.04)	1206 (85.96)	<0.001			
	2	Girl	415 (45.96)	197 (14.04)				
Father's education	1	Less high school	53 (6.10)	207 (14.84)	<0.001	30 (6.45)	188 (15.67)	<0.001
	2	High school	146 (16.80)	246 (17.63)		69 (14.84)	215 (17.92)	
	3	More high school	670 (77.10)	942 (67.53)		366 (78.71)	797 (66.42)	
Mother's education	1	Less high school	85 (9.85)	254 (18.22)	<0.001	39 (8.48)	226 (18.85)	<0.001
	2	High school	162 (18.77)	318 (22.81)		87 (18.91)	279 (23.27)	
	3	More high school	616 (71.38)	822 (58.97)		334 (72.61)	694 (57.88)	
Abortion history								
Induced abortion	1	Yes	230 (25.47)	590 (42.05)	<0.001	107 (21.93)	501 (41.54)	<0.001
	2	No	673 (74.53)	813 (57.95)		381 (78.07)	705 (58.46)	
Spontaneous abortion	1	Yes	45 (4.98)	126 (8.98)	<0.001	28 (5.74)	108 (8.96)	0.027
	2	No	858 (95.02)	1277 (91.02)		460 (94.26)	1098 (91.04)	
Adverse events during pregnancy								
Chemical exposure	1	Yes	15 (1.67)	119 (8.48)	<0.001	5 (1.03)	100 (8.29)	<0.001
	2	No	883 (98.33)	1284 (91.52)		480 (98.97)	1106 (91.71)	
Maternal infection	1	Yes	91 (10.12)	443 (31.58)	<0.001	57 (11.78)	382 (31.67)	<0.001
	2	No	808 (89.88)	960 (68.42)		427 (88.22)	824 (68.33)	
Other diseases	1	Yes	54 (5.98)	120 (8.55)	0.022	32 (6.56)	104 (8.62)	0.156
	2	No	849 (94.02)	1283 (91.45)		456 (93.44)	1102 (91.38)	
Use of medication	1	Yes	55 (6.09)	322 (22.95)	<0.001	32 (6.56)	277 (22.97)	<0.001
	2	No	848 (93.91)	1081 (77.05)		456 (93.44)	929 (77.03)	
Threaten abortion	1	Yes	51 (5.65)	213 (15.18)	<0.001	24 (4.92)	189 (15.67)	<0.001
	2	No	851 (94.35)	1190 (84.82)		464 (95.08)	1017 (84.33)	
Psychosocial stress								
Mild emotional problem	1	Yes	84 (9.30)	311 (22.17)	<0.001	46 (9.43)	266 (22.06)	<0.001
	2	No	819 (90.7)	1092 (77.83)		442 (90.57)	940 (77.94)	
Severe emotional problem	1	Yes	47 (5.24)	208 (14.83)	<0.001	25 (5.18)	175 (14.51)	<0.001
	2	No	850 (94.76)	1195 (85.17)		458 (94.82)	1031 (85.49)	
Traumatic event	1	Yes	41 (4.54)	168 (11.97)	<0.001	22 (4.51)	146 (12.11)	<0.001
	2	No	862 (95.46)	1235 (88.03)		466 (95.49)	1060 (87.89)	
Perinatal condition								
Term of delivery	0	NA	37 (4.10)	30 (2.14)	<0.001	24 (4.92)	24 (1.99)	<0.001
	1	Premature	34 (3.77)	121 (8.62)		19 (3.89)	109 (9.04)	
	2	Post term	24 (2.66)	84 (5.99)		12 (2.46)	70 (5.80)	
	3	Full term	808 (89.48)	1168 (83.25)		433 (88.73)	1003 (83.17)	
Method of delivery	1	Natural	369 (40.86)	477 (34.00)	<0.001	190 (38.93)	414 (34.33)	<0.001
	2	Cesarean	389 (43.08)	774 (55.17)		224 (45.90)	668 (55.39)	
	3	Assisted	144 (15.95)	152 (10.83)		73 (14.96)	124 (10.28)	
First delivery	1	Yes	765 (87.53)	1319 (94.01)	<0.001	409 (86.65)	1128 (93.53)	<0.001
	2	No	109 (12.47)	84 (5.99)		63 (13.35)	78 (6.47)	

Table S3. Summary of stepwise regression analysis of the combined sample

Effect	DF	Overall				boys-only			
		Main effect		Interaction		Main effect		Interaction	
		Wald Chi-Sq	P	Wald Chi-Sq	P	Wald Chi-Sq	P	Wald Chi-Sq	P
Demographics									
Residence	1	9.61	1.94x10 ⁻⁰³	9.41	2.16x10 ⁻⁰³				
Gender	1	203.03	4.55x10 ⁻⁴⁶	202.61	5.63x10 ⁻⁴⁶				
Father's education	2	31.77	1.26x10 ⁻⁰⁷	31.58	1.39x10 ⁻⁰⁷	29.33	4.27x10 ⁻⁰⁷	28.69	5.90x10 ⁻⁰⁷
Abortion history									
Induced abortion	1	40.04	2.49x10 ⁻¹⁰	39.71	2.95x10 ⁻¹⁰	35.64	2.37x10 ⁻⁰⁹	35.99	1.98x10 ⁻⁰⁹
Adverse events during pregnancy									
Chemical exposure	1	21.40	3.73x10 ⁻⁰⁶	22.05	2.65x10 ⁻⁰⁶	14.61	1.32x10 ⁻⁰⁴	15.66	7.56x10 ⁻⁰⁵
Maternal infection	1	41.65	1.09x10 ⁻¹⁰	39.64	3.05x10 ⁻¹⁰	19.86	8.33x10 ⁻⁰⁶	20.69	5.39x10 ⁻⁰⁶
Use of medication	1	36.56	1.48x10 ⁻⁰⁹	37.66	8.41x10 ⁻¹⁰	25.53	4.35x10 ⁻⁰⁷	22.55	2.05x10 ⁻⁰⁶
Threatened abortion	1	18.89	1.38x10 ⁻⁰⁵	21.02	4.53x10 ⁻⁰⁶	20.07	7.45x10 ⁻⁰⁶	21.68	3.22x10 ⁻⁰⁶
Psychosocial stress									
Severe emotional problem	1	19.85	8.39x10 ⁻⁰⁶	20.19	7.02x10 ⁻⁰⁶	9.29	2.31x10 ⁻⁰³	10.08	1.50x10 ⁻⁰³
Traumatic event	1	3.37	6.64x10 ⁻⁰²	3.14	7.63x10 ⁻⁰²	3.27	7.04x10 ⁻⁰²	2.96	8.55x10 ⁻⁰²
Perinatal conditions									
Term of delivery	2	23.00	1.01x10 ⁻⁰⁵	22.73	1.16x10 ⁻⁰⁵	16.71	2.36x10 ⁻⁰⁴	16.46	2.66x10 ⁻⁰⁴
Method of delivery	2	9.35	9.33x10 ⁻⁰³	9.20	1.00x10 ⁻⁰²	8.24	1.62x10 ⁻⁰²	8.37	1.52x10 ⁻⁰²
First delivery	1	37.07	1.14x10 ⁻⁰⁹	36.56	1.48x10 ⁻⁰⁹	31.45	2.05x10 ⁻⁰⁸	30.89	2.74x10 ⁻⁰⁸
Interaction									
Maternal infection * Use of medication	1			10.95	9.37x10 ⁻⁰⁴			10.40	1.26x10 ⁻⁰³